Pergamon

Tetrahedron 57 (2001) 4297–4309

TETRAHEDRON

A facile synthesis of 1′-*C*-alkyl-α-disaccharides from 1-*C*-alkyl-hexopyranoses and methyl 1-*C*-methyl-hexopyranosides

Xiaoliu Li, Hiro Ohtake, Hideyo Takahashi and Shiro Ikegami*

School of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-0195, Japan

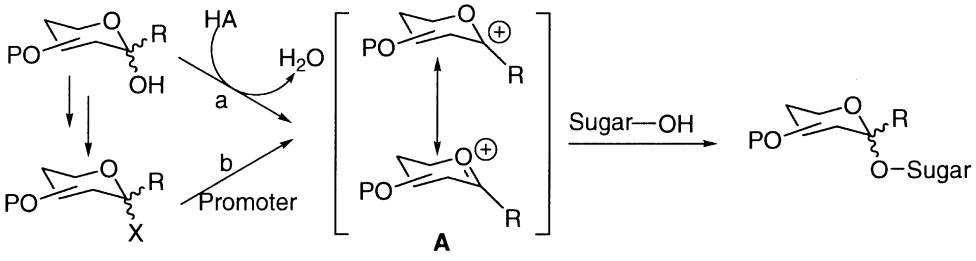
Received 27 December 2000; accepted 16 March 2001

Abstract—Direct *O*-glycosidations using the 1-*C*-alkyl-2,3,4,6-tetra-*O*-benzyl-hexopyranoses as the glycosyl donors were carried out with a catalytic amount (0.2 equiv.) of trimethylsilyl trifluoromethanesulfonate (TMSOTf). The glycosidations proceeded α-stereoselectively and furnished the corresponding 1′-*C*-alkyl-α-disaccharides in 71–90% yields. The *O*-transglycosidations from the benzylated and acetylated methyl 1-*C*-methyl-α-hexopyranosides to the corresponding 1′-*C*-methyl-α-*O*-disaccharides were also examined, respectively. These transglycosidations took place on α-stereoselectivity and provided the 1′-*C*-methyl-α-*O*-disaccharides as the sole products, implying that no neighboring group participation occured in the reactions.

1. Introduction

The important biological significance and potential chemotherapeutic value of carbohydrate compounds have stimulated much research activity on glycoside synthesis in the recent years.[1] Along with the achievements in the synthesis of complex saccharides, new methodologies for stereoselective glycosylations have been developed.[2] For the conventional methods, the anomeric centers of glycosyl donors are activated by conversion to the suitable derivatives, such as halides,[3] trichloroacetimidates,[4] thioglycosides,[5] phosphorous-containing living groups,[6] sulfoxides,[7] pentenylglycosides,[8] glycals,[9] etc., from which the intermediate **A** [Scheme 1(b), in the case of aldopyranose (R=H)], an oxocarbenium ion is generated in the presence of proper promoter and then followed by the combination of **A** (R=H) with a sugar alcohol in a stereospecific manner to afford the desired *O*-glycosides stereoselectively. However, direct glycosidation using 1-hydroxyaldopyranoses as the glycosyl donors showed less stereoselectivity [Scheme 1(a), in the case of aldopyranose (R=H)].[10]

We have reported an extremely efficient method for synthesizing 1′-*C*-methyl-α-*O*-disaccharides by the direct glycosidation of 1-methylenesugars and sugar alcohols in the presence of a catalytic amount of Lewis acid.[11] The *O*-glycosidation reaction showed α-stereoselectivity with no neighboring group participation. It was noted that the stereoselective glycosidations of 1-*C*-alkyl-hexopyranoses has not been investigated extensively, although recent methods for the glycosidations of 1-*C*-alkyl-hexopyranoses have been described which employed the similar activated derivatives as those for aldopyranoses [Scheme 1(b), in the case of ketopyranose (R=Alkyl)].[12] In light of this, we explored the stereoselective *O*-glycosidation of



Scheme 1. P, protecting group; HA, Lewis acid; X=F, Cl, Br, $OC(NH)CCl_3$, SPh, SEt, S(O)Ph, SO_2Ph, $OP(O)(OR)_2$, $OP(O)(NMe)_2$, $O(CH_2)_3CH{=}CH_2$, etc.; Aldopyranose: R=H, Ketopyranose: R=Alkyl.

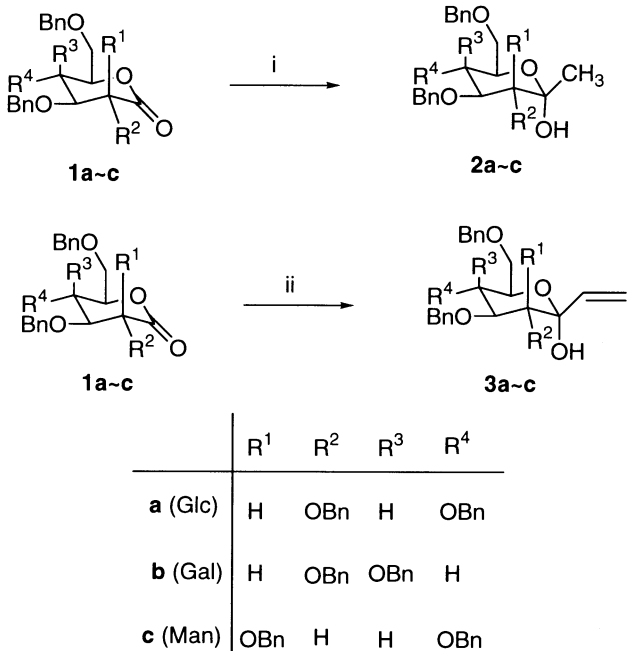
Keywords: 1-*C*-alkyl-hexopyranoses; methyl 1-*C*-methyl-α-hexopyranosides; 1′-*C*-alkyl-α-disaccharides; *O*-glycosidation; *O*-transglycosidation.
* Corresponding author. Tel.: +81-426-85-3728; fax: +81-426-85-1870; e-mail: shi-ike@pharm.teikyo-u.ac.jp

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00321-0

1-*C*-alkyl-hexopyranoses [Scheme 1(a), in the case of ketopyranose (R=Alkyl)] to investigate the differences between aldopyranoses and ketopyranoses.

2. Results and discussion

1-*C*-alkyl-hexopyranoses could be readily prepared by reactions of the corresponding hexopyranolactones with organometallic reagents,[13] for example, the Reformatsky-type reactions[14] or the reactions with Grignard reagents[15] or organolithium reagents.[15a,16] However, in most cases the formed ketopyranoses were directly used to synthesize modified sugars, especially *C*-glycosides by reductive treatment with triethylsilane and boron trifluoride etherate,[15a,16a,16c] and very little detailed analytical data for the 1-*C*-alkyl-hexopyranose compounds has been reported. Thus, the starting materials, 1-hydroxy-1-*C*-methyl-hexopyranoses (**2a–c**), were conveniently prepared by the reaction of the corresponding lactones **1a–c**[17] with methyllithium (1.2 equiv.) in THF solution at −78°C in yields of 83–97% as shown in Scheme 2. Similarly, the 1-hydroxy-1-*C*-vinyl-hexopyranoses **3a–c** were obtained from the reaction of lactones **1a–c** and vinylmagnesium bromide in good yields. The analytical data for the products **2** and **3** are listed in the Experimental section.

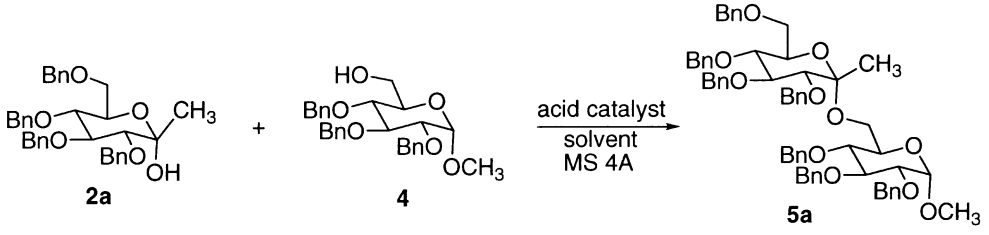


	R^1	R^2	R^3	R^4
a (Glc)	H	OBn	H	OBn
b (Gal)	H	OBn	OBn	H
c (Man)	OBn	H	H	OBn

Scheme 2. *Reagents and conditions*: (i) CH_3Li (1.2 equiv.), THF, −78°C; (ii) CH_2=CHMgBr (1.5 equiv.), THF, −78°C.

While the *O*-glycosidations of aldopyranoses with both activated and nonactivated anomeric centres have been well documented,[2–8,10] there has been, to the best of our knowledge, no report on the *O*-glycosidation using 1-*C*-alkyl-hexopyranoses as the glycosyl donors. Thus, we first investigated the conditions for the *O*-glycosidations using **2a**, employing the methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **4**[18] as the glycosyl acceptor (Scheme 3). The results are summarized in Table 1.

Considering the excellent yields of disaccharides in the *O*-glycosidation of 1-methylenesugars promoted by trifloromethanesulfonic acid (TfOH),[11] we examined the *O*-glycosidation of **2a** under the same conditions as that of the 1-methylenesugar reactions. We found that the *O*-glycosidation did not complete well at −78°C even using 1.5 equiv. of TfOH (entry 1), with the starting material **2a** remaining unreacted after 3 h. Increasing reaction temperature brought about side reactions and did not improve the



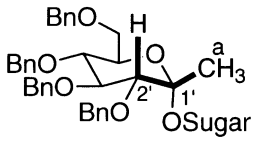
Scheme 3.

Table 1. The glycosidation of the 1-*C*-methyl-glucopyranose **2a** with the sugar alcohol **4**

Entry	Catalyst (equiv.)	Solvent	Conditions	Yield of **5a** (%)
1	TfOH (1.5)	CH_2Cl_2	−78°C, 3 h	75.1[a]
2	TfOH (1.0)	CH_2Cl_2	−78°C, 1 h; 0°C, 1 h	78.5
3	TMSOTf (0.05)	CH_2Cl_2	0°C, 4 h	71.7[a]
4	TMSOTf (0.2)	CH_2Cl_2	0°C, 2 h	90.3
5	TMSOTf (0.5)	CH_2Cl_2	0°C, 2 h	86.2
6	TMSOTf (1.0)	CH_2Cl_2	0°C, 2 h	79.8
7	TMSOTf (0.5)	Et_2O	0°C, 4 h	83.1
8	TMSOTf (0.5)	THF	0°C, 4 h	80.9
9	BF_3·Et_2O (1.0)	CH_2Cl_2	0°C, 2 h	77.9
10	$SnCl_4$ (1.0)	CH_2Cl_2	0°C, 2 h	70.3
11	$TiCl_4$ (1.0)	CH_2Cl_2	0°C, 2 h	73.8
12	$ZnCl_2$ (1.0)	CH_2Cl_2	0°C, 4 h	76.6[a]

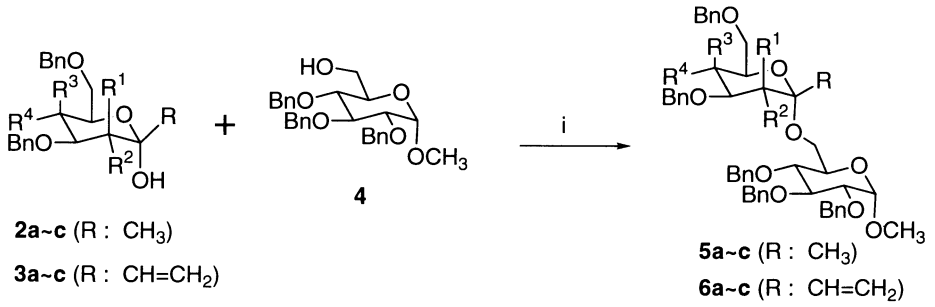
[a] The starting material **2a** was partly recovered.

yield markedly (entry 2). The results indicated that TfOH was not as effective for promoting the *O*-glycosidation of the 1-*C*-alkyl-hexopyranoses **2** as it was for catalyzing the glycosidation of 1-methylenesugars.[11] After screening the reaction with a variety of Lewis acid catalysts (Table 1), it was found that trimethylsilyl trifluoromethanesulfonate (TMSOTf) was most effective for this glycosidation. Although the reactions gave the disaccharide **5a** in moderate yields with both a low equivalent molar ratio (entry 3) and high ratios (entry 5 and 6) of the catalyst, excellent yield (90.3%) for the *O*-glycosidation was achieved using a catalytic amount (0.2 equiv.) of TMSOTf in dichloromethane at 0°C in the presence of molecular sieves 4A (entry 4). It should be noteworthy that the *O*-glycosidation of the 1-*C*-methyl-glucopyranose **2a** took place stereoselectively and provided the α-disaccharide **5a** as the sole product. In addition, it was found that the solvent did not have much effect on the glycosidation yield and the stereochemistry



$^3J_{H\text{-}2',C\text{-}a} = 1.73$ Hz

Figure 1.



2a~c (R : CH_3)

3a~c (R : $CH{=}CH_2$)

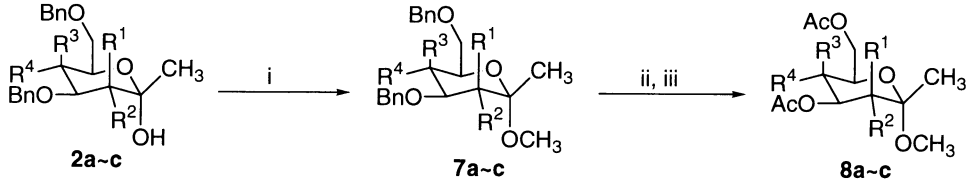
4

5a~c (R : CH_3)

6a~c (R : $CH{=}CH_2$)

	R^1	R^2	R^3	R^4	Yield of **5** (%)	Yield of **6** (%)
a (Glc)	H	OBn	H	OBn	90.3	88.3
b (Gal)	H	OBn	OBn	H	89.1	71.0
c (Man)	OBn	H	H	OBn	86.8	78.0

Scheme 4. *Reagents and conditions*: (i) TMSOTf (0.2 equiv.), MS 4A, CH_2Cl_2, 0°C.



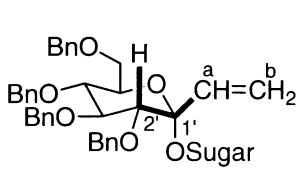
2a~c

7a~c

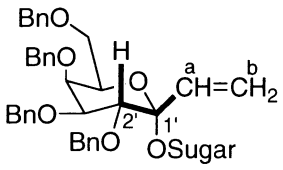
8a~c

	R^1	R^2	R^3	R^4	Yield (%)
7a (Glc)	H	OBn	H	OBn	91.5
7b (Gal)	H	OBn	OBn	H	95.1
7c (Man)	OBn	H	H	OBn	92.4
8a (Glc)	H	OAc	H	OAc	88.2
8b (Gal)	H	OAc	OAc	H	85.1
8c (Man)	OAc	H	H	OAc	87.5

Scheme 5. *Reagents and conditions*: (i) MeOH, TMSOTf (0.2 equiv.), $MgSO_4$, CH_2Cl_2, 0°C; (ii) $Pd(OH)_2$ /C, H_2, MeOH, r.t.; (iii) Ac_2O, pyridine, r.t., overnight.



6a ($^3J_{H\text{-}2',C\text{-}a}$ = 1.1 Hz)



6b ($^3J_{H\text{-}2',C\text{-}a}$ = 1.0 Hz)

Figure 2.

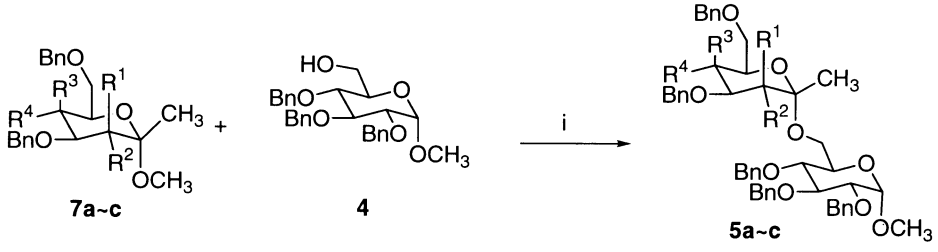
(entry 5, 7, 8). Under the same conditions, the *O*-glycosidations of **2b** and **2c** with **4** were performed and furnished the corresponding α-disaccharides **5b** and **5c**, respectively (Scheme 4). The structures and the α-configurations of the disaccharides **5** were determined by the comparison of their ^{1}H NMR and ^{13}C NMR spectra and the three bond coupling constants $^3J_{H\text{-}2',Me\text{-}1'}$ between the H-2′ and the carbon of 1′-*C*-methyl with those of the known compounds prepared from 1-methylenesugars (Fig. 1).[11]

Following the above described procedure, the *O*-glycosidations of the 1-hydroxy-1-*C*-vinyl-hexopyranoses **3a–c** with the methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **4** were carried out. The reactions proceeded smoothly using a catalytic amount (0.2 equiv.) of TMSOTf at 0°C and provided exclusively the corresponding α-disaccharides **6a–c** in good yields (Scheme 4). Similarly, the glycosidations of the compounds **2a–c** with methanol in the presence of 0.2 equiv. of TMSOTf using anhydrous magnesium sulfate ($MgSO_4$) as the dehydrating reagent gave the corresponding methyl 1-*C*-methyl-hexopyranosides **7a–c**[19] in excellent yields (Scheme 5).

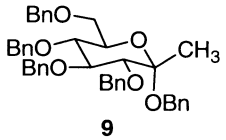
The structures of the compounds **6** and **7** were determined by analyses of their spectral data of ^{1}H NMR, ^{13}C NMR, 2D-COSY and MS (FAB$^+$). With the similar method to the previous paper,[11] the conformations of 1′-anomeric carbons in **6a** and **6b** were tentatively determined according to the three bond coupling constant $^3J_{H\text{-}2',C\text{-}a}$ between H-2′ and C-a of the vinyl group (Fig. 2). The coupling constants, 1.1 and 1.0 Hz for **6a** and **6b,** respectively, showed synclinal arrangements between the 2′-proton and the 1′-*C*-vinyl group, indicating α-configurations of the 1′-anomeric carbons.

In order to examine the scope of the glycosidation of ketopyranoses whose high reactivity and stereoselectivity may result from the formation of the stable intermediate **A** [Scheme 1, in the case of ketopyranose (R=Alkyl)], we explored the *O*-transglycosidation using the methyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-hexopyranosides **7a–c** as the glycosyl donors and the methyl 2,3,4-tri-*O*-benzyl-α-D-glucoside **4** as the glycosyl acceptor. In the reaction, the 1-*C*-methyl-hexopyranosyl moiety was transferred to the acceptor **4** with the replacement of the methoxy group, affording the 1′-*C*-methyl-disaccharides **5a–c** (Scheme 6).

Although the 1-*C*-alkyl-hexopyranoses and 1-methylensugars were liable to form the oxocarbenium ion intermediate **A** [Scheme 1, ketopyranose (R=Alkyl)] in the



	R^1	R^2	R^3	R^4	Yield of **5** (%)
a (Glc)	H	OBn	H	OBn	80.6
b (Gal)	H	OBn	OBn	H	78.1
c (Man)	OBn	H	H	OBn	86.8



9

Scheme 6. *Reagents and conditions*: (i) $SnCl_4$ (1.0 equiv.), MS 4A, CH_2Cl_2, 0°C, 3 h.

Table 2. The *O*-transglycosidation of the methyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methylglucoside **7a** with the sugar alcohol **4**

Entry	Catalyst (equiv.)	Conditions	**5a** (%)	**9** (%)	**7a** (%)
1	TfOH (0.5)	0°C, 2 h	31.2	12.1	19.7
2	TMSOTf (1.0)	0°C, 3 h	33.4	8.2	36.5
3	$BF_3{\cdot}Et_2O$ (1.0)	0°C, 3 h	36.2	9.1	32.9
4	$SnCl_4$ (0.5)	0°C, 3 h	60.6	–	28.2
5	$SnCl_4$ (1.0)	0°C, 3 h	80.6	–	6.8
6	$SnCl_4$ (1.5)	0°C, 3 h	71.3	5.8	–
7	$SnCl_4$ (1.0)	0°C, 5 h	73.7	5.6	–
8[a]	$SnCl_4$ (1.0)	0°C, 3 h	65.6	3.4	13.1
9	$AlCl_3$ (1.0)	r.t., 3 h	40.8	9.5	20.0
10	$TiCl_4$ (1.0)	0°C, 3 h	62.8	4.2	15.6
11	$ZnCl_2$ (2.0)	r.t., 4 h	28.3	–	58.8

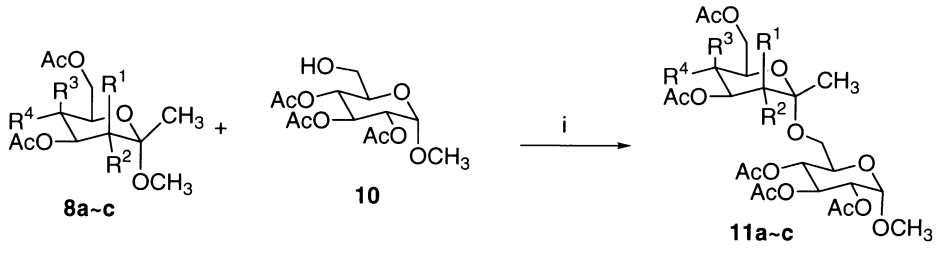
[a] Without molecular sieves.

glycosidations catalyzed by Lewis acids, but the methyl 1-*C*-methyl-hexopyranosides **7** did not easily generate the intermediate **A** due to the higher stability of the methyl glycosidic ether bond.[20] Therefore, several stronger Lewis acids such as $TiCl_4$, $ZnCl_2$, TMSOTf, $SnCl_4$, $BF_3{\cdot}Et_2O$, $AlCl_3$, and TfOH were examined for their ability to catalyze the *O*-transglycosidation of **7a** (Table 2). It was found that under the catalysis of the strong Lewis acids the *O*-transglycosidation took place affording the disaccharide **5a** (Scheme 6) as did with the main side reaction forming the by-product **9**.[11] The results showed that the Lewis acids TMSOTf, TfOH, $ZnCl_2$, $BF_3{\cdot}Et_2O$ and $AlCl_3$ were not effective for catalyzing the transglycosidation reaction (Entries 1–3, 9 and 11). However, the reaction under the catalysis of $SnCl_4$ provided better yields than that catalyzed by $TiCl_4$ even though the transglycosidations did not proceed to completion in both cases. In addition, molecular sieves was necessary for improving the transglycosidation by removing the generated methanol from the reaction system (Entry 8). Thus, the *O*-transglycosidation of **7a** and **4** was found to proceed well under the catalysis of $SnCl_4$ (1.0 equiv.) in the presence of MS 4A at 0°C and furnished the disaccharide **5a** in 80.6% yield (Entry 5). Similarly, the transglycosidations of **7b–c** and **4** were carried out under the same conditions to afford **5b–c** in good yields.

The *O*-transglycosidations of the acetyl protected methyl 1-*C*-methyl-hexopyranosides **8a–c** and **10**[21] were performed in order to examine the neighboring group participation effect (Scheme 7). Compared with the benzyl-protected glycosides, the acetyl-protected glycosides exhibited lower reactivity to glycosidation.[11] We thought that stronger conditions might benefit the reaction. The *O*-transglycosidations of **8a–c** and **10**, after scanning several Lewis acids, were found to occur most favourably in the presence of an excess amount (4.0 equiv.) of $SnCl_4$ and afforded the corresponding α-disaccharides **11a–c**, respectively. It was observed that under the strong conditions, acetyl group migration occurred in the compound **10** accompanyed by the transglycosidation, leading in the low yields of the disaccharides **11**.[22] The spectral data showed that the conformations of the disaccharides **11** were identical to those of the corresponding known compounds,[11] implying that no neighboring group participation was present in the transglycosidations.

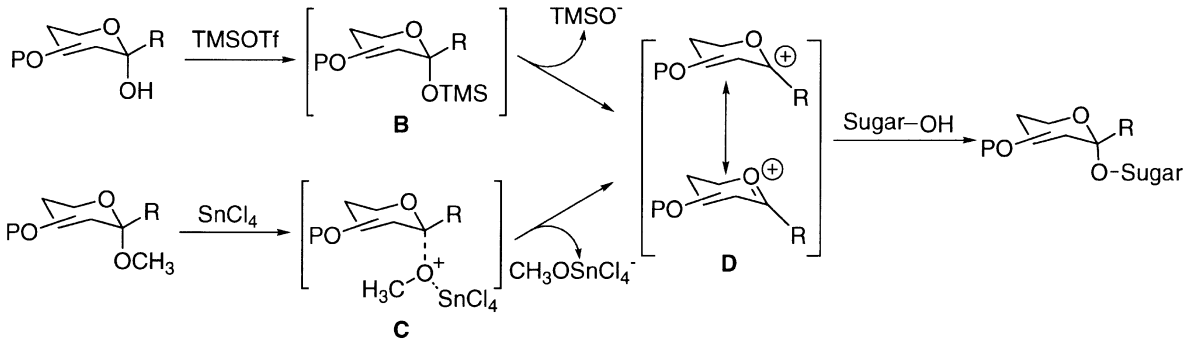
The successful *O*-transglycosidations substituting methoxy groups as in **7** and **8** with glycosyl acceptors supported the reaction mechanism shown in Scheme 8. In the glycosidations and the transglycosidations, the stable intermediate **D** (a tertiary oxocarbenium ion) was generated from **B** or **C**, and then combined with sugar alcohols to form the α-*O*-glycosides.[11] The stability of the tertiary oxocarbenium ion **D** resulted in the α-stereoselectivity in the glycosidations due to the anomeric effect and made the *O*-transglycosidations possible.

Ulosonic acid derivatives, especially, the sialic acid glycosides play important roles in various biological processes,[23] and syntheses of sialyl glycosides and their analogues have been well documented.[24] Generally, the glycosidations of sialic acid derivatives did not proceed as smoothly as those of aldopyranoses due to a reduction in the reactivity of the anomeric center caused by the steric and electronic properties of the carboxyl group. In addition, owing to the anomeric effects, the *O*-glycosidations of the sialic acid derivatives tended to form the β-anomer which is contrary to natural sialic acid glycosides.[24c] As the further

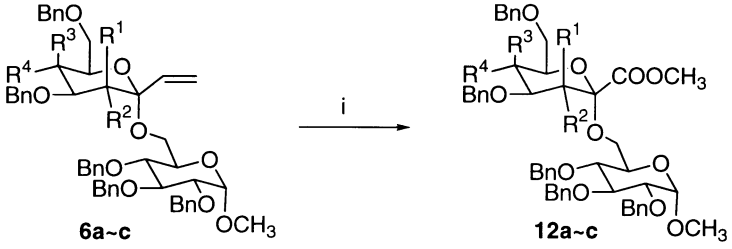


	R^1	R^2	R^3	R^4	Yield of **11** (%)
a (Glc)	H	OAc	H	OAc	30.1
b (Gal)	H	OAc	OAc	H	63.0
c (Man)	OAc	H	H	OAc	82.8

Scheme 7. *Reagents and conditions*: (a) $SnCl_4$ (4.0 equiv.), MS 4A, 0°C, CH_2Cl_2, 2 h, then r.t., 1 h.



Scheme 8. P, protecting group, R=Alkyl.



	R^1	R^2	R^3	R^4	Yield of **12** (%)
a (Glc)	H	OBn	H	OBn	32.5
b (Gal)	H	OBn	OBn	H	30.2
c (Man)	OBn	H	H	OBn	31.1

Scheme 9. *Reagents and conditions*: (i) NaOH / MeOH, CH_2Cl_2, O_3, −78°C.

applications of the α-stereoselective 1-*C*-alkyl-hexopyranosyl glycosidation described above, we envisaged to synthesize ulosonyl glycoside derivatives employing the 1′-*C*-vinyldisaccharides **6** in which the vinyl group serves as the precursor to the carboxylate group by α-*O*-glycosidation of 1-*C*-vinyl-hexopyranosides **3** (Scheme 4) followed by cleavage of the olefinic bond into a carboxylate group (Scheme 9).

While transformation of olefinic bonds into carboxyl groups has been well developed,[25] considering the 1′-*C*-vinyldisaccharides **6** being sensitive to strong acidic conditions and stable to basic conditions, we tried conversing **6** to **12** by a modification of Marshall′s method involving ozonolysis of the olefinic bond at −78°C in a solution of sodium hydroxide–methanol and dichloromethane.[26] Using this method the corresponding methyl esters **12** were obtained directly from **6**. Since 1-*C*-alkyl-hexopyranoses having different functional groups can be conveniently prepared by reaction of the corresponding sugar lactones with organometallic reagents, it is possible to synthesize 1′-*C*-alkyl-α-*O*-disaccharides containing a functional group by the present *O*-glycosidation method.

In summary, direct *O*-glycosidation using 1-*C*-alkyl-hexopyranoses as glycosyl donors proceeded smoothly with a catalytic amount of TMSOTf, providing a facile method for the synthesis of 1′-*C*-alkyl-α-disaccharides from sugar lactones. The *O*-transglycosidations of methyl 1-*C*-methyl-hexopyranosides were also achieved under the promotion of the Lewis acid, $SnCl_4$. Both of these reactions showed α-stereoselectivity and no neighboring group participation. Applications of the α-stereoselectivity of these *O*-glycosidations for synthesis are being explored.

3. Experimental

3.1. General methods

Melting points were measured on a YANACO Micro Melting Point Apparatus and are uncorrected. IR spectra were recorded on a Jasco FT/IR-800 Fourier-transform infrared spectrometer. ^{1}H-NMR, ^{13}C-NMR and 2D-COSY spectra, and the three bond coupling constants $^3J_{H,C}$ were measured on a JEOL JNM-GSX400 (400 MHz) and a JEOL-ECP600 (600 MHz) pulse Fourier-transform NMR spectrometers in $CDCl_3$ solution using tetramethylsilane (Me_4Si) as an internal standard. Mass spectra (MS) and high resolution mass spectra (HRMS) were carried out on

a JEOL JMS-SX102A mass spectrometer using FAB (Fast Atomic Bombardment). Optical rotations were measured with a Jasco DIP-370 digital polarimeter. Thin-layer chromatography (TLC) was performed on precoated plates (Merck TLC aluminum sheets silica 60 F_{254}) with detection by UV light or with phosphomolybdic acid in EtOH/H_2O followed by heating. Column chromatography was performed using SiO_2 (Wakogel C-200, Wako). Ozone was generated by an O-3-2 type Ozone generator (Nippon Ozone Co., Ltd.) using O_2 as the oxygen supply.

3.1.1. 2,3,4,6-Tetra-*O*-benzyl-1-*C*-methyl-α-D-glucopyranose (2a). To a solution of 2,3,4,6-tetra-*O*-benzylglucono-1,5-lactone (**1a**) (2.69 g, 5.0 mmol) in 25 mL of dry THF was added 6.0 mL of methyl lithium in ethyl ether (1.0 mol/L) (1.2 equiv.) at −78°C under argon atmosphere. The solution was stirred for 1 h and the reaction was quenched with water. The mixture was extracted with AcOEt. The organic phase was washed with water (100 mL×3), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was submitted to a silica gel column chromatography using Et_2O: Hexane=1:1 (v/v) as the eluent to afford product **2a**, (2.30 g, 83.0%). White solid, mp: 92–93°C; $[\alpha]_D^{24}$: +24.7° (*c* 1.0, $CHCl_3$); IR (KBr): 3464.57, 3063.33, 3030.54, 2932.16, 2903.22, 2868.50, 1603.04, 1585.68, 1496.94, 1454.50, 1404.35, 1363.84, 1199.87, 1153.57, 1086.06, 1043.62, 1028.18, 976.10, 871.93, 850.71, 760.05, 738.83, 698.32 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.39 (s, 3H, CH_3), 2.86 (s, br, 1H, OH), 3.35 (d, 1H, *J*=9.46 Hz, 2-H), 3.64 (t, 1H, *J*=9.77 Hz, 4-H), 3.64–3.66 (d, 1H, 6-H, overlapped with 4-H), 3.70 (dd, 1H, *J*=10.68 Hz, *J*=4.27 Hz, 6-H), 3.98 (t, 1H, *J*=9.15 Hz, 3-H), 3.99–4.05 (m, 1H, 5-H), 4.50 (d, 1H, *J*=12.21 Hz, CH_2Ph), 4.55 (d, 1H, *J*=10.99 Hz, CH_2Ph), 4.59 (d, 1H, *J*=12.21 Hz, CH_2Ph), 4.69 (d, 1H, *J*= 10.99 Hz, CH_2Ph), 4.82 (d, 1H, *J*=10.98 Hz, CH_2Ph), 4.88 (s, 2H, CH_2Ph), 4.92 (d, 1H, *J*=11.29 Hz, CH_2Ph), 7.14–7.16 (m, 2H, ArH), 7.24–7.33 (m, 18H, ArH); ^{13}C NMR ($CDCl_3$): δ 26.57 (CH_3), 68.83 (6-C), 71.53 (5-C), 73.41 (CH_2Ph), 74.82 (CH_2Ph), 75.56 (CH_2Ph), 75.66 (CH_2Ph), 78.45 (4-C), 83.19 (3-C), 83.62 (2-C), 97.35 (1-C), 127.57 (Ph), 127.63 (Ph), 127.72 (Ph), 127.80 (Ph), 127.82 (Ph), 127.89 (Ph), 127.95 (Ph), 128.27 (Ph), 128.32 (Ph), 128.33 (Ph), 128.40 (Ph), 137.88 (Ph), 138.22 (Ph), 138.26 (Ph), 138.65 (Ph); HRMS (FAB): calcd for $C_{35}H_{38}O_6Na$ 577.2566, found 577.2564.

3.1.2. 2,3,4,6-Tetra-*O*-benzyl-1-*C*-methyl-α-D-galactopyranose (2b). Following the procedure used to prepare **2a**, the compound **2b** was prepared from 2.69 g (5.0 mmol) of 2,3,4,6-tetra-*O*-benzylgalactono-1,5-lactone (**1b**) and 6.0 mL of methyl lithium in ethyl ether (1.0 mol/L) (1.2 equiv.). The syrupy product **2b** was obtained, 2.36 g (85.2%). $[\alpha]_D^{23}$: +22.0° (*c* 1.0, $CHCl_3$); IR (neat): 3443.36, 3063.33, 3030.54, 2920.58, 2870.34, 1604.97, 1585.68, 1496.94, 1454.50, 1365.77, 1205.66, 1097.63, 1028.18, 736.90, 698.31 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (s, 3H, CH_3), 2.61 (s, br, 1H, OH), 3.51–3.59 (m, 2H, two 6-H), 3.81 (d, 1H, *J*=9.76 Hz, 2-H), 3.89 (dd, 1H, *J*=9.46 Hz, *J*=3.44 Hz, 3-H), 4.00 (d, 1H, *J*=2.44 Hz, 5-H), 4.11 (t, 1H, *J*=7.02 Hz, 4-H), 4.43 (d, 1H, *J*=12.20 Hz, CH_2Ph), 4.48 (d, 1H, *J*=11.90 Hz, CH_2Ph), 4.61 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.66–4.75 (m, 3H, CH_2Ph), 4.93 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.97 (d, 1H, *J*=10.99 Hz, CH_2Ph), 7.24–7.36 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 26.59 (CH_3), 68.83 (6-C), 70.18 (5-C), 72.38 (CH_2Ph), 73.40 (CH_2Ph), 74.30 (4-C), 74.45 (CH_2Ph), 75.75 (CH_2Ph), 79.76 (2-C), 80.92 (3-C), 97.84 (1-C), 127.48 (Ph), 127.49 (Ph), 127.55 (Ph), 127.68 (Ph), 127.74 (Ph), 127.89 (Ph), 128.03 (Ph), 128.16 (Ph), 128.30 (Ph), 128.34 (Ph), 128.38 (Ph), 138.00 (Ph), 138.15 (Ph), 138.45 (Ph), 138.82 (Ph); HRMS (FAB): calcd for $C_{35}H_{38}O_6Na$ 577.2566, found 577.2570.

3.1.3. 2,3,4,6-Tetra-*O*-benzyl-1-*C*-methyl-α-D-mannopyranose (2c). Following the procedure used to prepare **2a**, the compound **2c** was prepared from 2.69 g (5.0 mmol) of 2,3,4,6-tetra-*O*-benzylmannono-1,5-lactone (**1c**) and 6.0 mL of methyl lithium in ethyl ether (1.0 mol/L) (1.2 equiv.). The syrupy product **2c** was obtained, 2.70 g (97.6%). $[\alpha]_D^{23}$: +14.8° (*c* 1.0, $CHCl_3$); IR (neat): 3418.28, 3063.33, 3030.54, 2918.20, 2866.57, 1604.97, 1585.68, 1496.94, 1454.50, 1367.70, 1205.66, 1089.91, 902.80, 738.83, 696.39 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (s, 3H, CH_3), 2.95 (s, br, 1H, OH), 3.61–3.73 (m, 2H, two 6-H), 3.69 (d, 1H, *J*=2.75 Hz, 2-H, overlaped with 6-H), 3.84 (t, 1H, *J*=9.46 Hz, 4-H), 3.94–3.99 (m, 1H, 5-H), 4.12 (dd, 1H, *J*=9.46 Hz, *J*=2.75 Hz, 3-H), 4.51 (d, 1H, *J*=10.99 Hz, CH_2Ph), 4.55 (d, 2H, *J*=5.49 Hz, CH_2Ph), 4.66 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.73 (s, 2H, CH_2Ph), 4.85 (d, 1H, *J*=10.99 Hz, CH_2Ph), 4.95 (d, 1H, *J*=11.60 Hz, CH_2Ph), 7.15–7.38 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 26.30 (CH_3), 69.73 (6-C), 72.52 (5-C), 72.55 (CH_2Ph), 73.22 (CH_2Ph), 74.69 (CH_2Ph), 74.86 (CH_2Ph), 75.06 (2-C), 78.14 (4-C), 81.43 (3-C), 98.03 (1-C), 127.42 (Ph), 127.48 (Ph), 127.86 (Ph), 127.92 (Ph), 127.97 (Ph), 128.01 (Ph), 128.12 (Ph), 128.22 (Ph), 128.32 (Ph), 138.28 (Ph), 138.39 (Ph), 138.53 (Ph), 138.61 (Ph); HRMS (FAB): calcd for $C_{35}H_{38}O_6Na$ 577.2566, found 577.2561.

3.1.4. 2,3,4,6-Tetra-*O*-benzyl-1-*C*-vinyl-α-D-glucopyranose (3a). 1.58 mL of Vinyl magnesium bromide (1.5 equiv.) in THF (0.95 mol/L) was added to a solution of 538 mg (1.0 mmol) of 2,3,4,6-tetra-*O*-benzylglucono-1,5-lactone (**1a**) in 10 mL of dry THF at −78°C under argon atmosphere. The solution was stirred for 1 h, then the reaction temperature raised gradually up to 0°C, and the reaction was quenched with water. The mixture was extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by silica gel column chromatography (Et_2O-Hexane 1:1 v/v) to provide **3a** (462 mg, 81.6%). Colorless syrup; $[\alpha]_D^{22}$: +42.9° (*c* 1.0, $CHCl_3$); IR (neat): 3418.28, 3063.33, 3030.54, 2920.58, 2866.57, 1952.20, 1875.04, 1811.38, 1604.97, 1587.61, 1496.94, 1454.50, 1361.91, 1209.51, 1070.62, 1028.18, 991.53, 939.54, 850.71, 734.97, 698.32 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.79 (s, br, 1H, OH), 3.44 (d, 1H, *J*=9.16 Hz, 2-H), 3.69 (dd, 1H, *J*=10.07 Hz, *J*=2.14 Hz, 6-H), 3.79 (t, 1H, *J*=9.46 Hz, 4-H), 3.77 (dd, 1H, *J*=10.68 Hz, *J*=3.97Hz, 6-H), 3.98 (t, 1H, *J*=9.16 Hz, 3-H), 4.06 (ddd, 1H, *J*=10.07 Hz, *J*=3.97 Hz, *J*=1.83 Hz, 5-H), 4.51–4.66 (m, 4H, CH_2Ph), 4.76–4.84 (m, 2H, CH_2Ph), 4.88 (2s, br, 2H, overlapped, CH_2Ph), 5.30 (dd, 1H, *J*=10.68 Hz, *J*=1.22 Hz, CH_2=), 5.61 (dd, 1H, *J*=17.39 Hz, *J*=1.22 Hz, CH_2=), 6.00 (dd, 1H, *J*=17.39 Hz,

J=10.68 Hz, -CH=), 7.16–7.33 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 68.81 (6-C), 71.72 (5-C), 73.42 (CH_2Ph), 74.91 (CH_2Ph), 75.65 (two C, CH_2Ph), 78.16 (4-C), 82.75 (3-C), 83.39 (2-C), 96.51 (1-C), 117.18 (CH_2=), 127.55 (Ph), 127.59 (Ph), 127.64 (Ph), 127.72 (Ph), 127.76 (Ph), 127.82 (Ph), 127.85 (Ph), 128.23 (Ph), 128.31 (Ph), 128.34 (Ph), 128.36 (Ph), 137.77 (Ph), 138.26 (Ph), 138.66 (Ph), 138.76 (-CH=); HRMS (FAB): calcd for $C_{36}H_{38}O_6Na$ 589.2566, found 589.2563.

3.1.5. 2,3,4,6-Tetra-*O*-benzyl-1-*C*-vinyl-α-D-galactopyranose (3b). Following the procedure of preparing **3a**, 2,3,4,6-tetra-*O*-benzylgalactono-1,5-lactone (**1b**) (640 mg, 1.2 mmol) reacted with vinyl magnesium bromide (1.5 equiv.) to provide the compound **3b** (565 mg, 83.2%). Colorless syrup; $[\alpha]_D^{24}$: +32.5° (*c* 1.0, $CHCl_3$); IR (neat): 3406.55, 3063.33, 3030.54, 2922.08, 2868.22, 1604.97, 1496.94, 1454.50, 1361.92, 1209.51, 1073.02, 941.46, 736.72, 698.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.90 (s, br, 1H, OH) 3.53–3.62 (m, 2H, two 6-H), 3.87, (d, 1H, J=9.77 Hz, 2-H), 3.91 (dd, 1H, J =9.77 Hz, J=2.44 Hz, 3-H), 4.01 (s, br, 1H, 4-H), 4.10 (ddd, 1H, J=11.59 Hz, J=5.57 Hz, J=2.45 Hz, 5-H), 4.44 (d, 2H, J=6.71 Hz, CH_2Ph), 4.62 (d, 2H, J=10.68 Hz, CH_2Ph), 4.72 (s, 2H, CH_2Ph), 4.82 (d, 1H, J=10.68 Hz, CH_2Ph), 4.94 (dd, 1H, J=11.59 Hz, CH_2Ph), 5.26 (dd, 1H, J=10.38 Hz, J=0.92 Hz, CH_2=), 5.57 (dd, 1H, J=17.40 Hz, J=0.92 Hz, CH_2=), 5.99 (dd, 1H, J=17.40 Hz, J=10.68 Hz, -CH=), 7.26–7.34 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 68.72 (6-C), 70.35 (5-C), 72.67 (CH_2Ph), 73.38 (CH_2Ph), 74.48 (CH_2Ph), 74.49 (4-C), 75.72 (CH_2Ph), 79.10 (3-C), 80.57 (2-C), 96.91 (1-C), 116.93 (CH_2=), 127.46 (Ph), 127.59 (Ph), 127.79 (Ph), 127.97 (Ph), 128.15 (Ph), 128.19 (Ph), 128.28 (Ph), 128.33 (Ph), 137.97 (Ph), 138.06 (Ph), 138.50 (Ph), 138.82 (two C, -CH= and Ph); HRMS (FAB): calcd for $C_{36}H_{38}O_6Na$ 589.2566, found 589.2558.

3.1.6. 2,3,4,6-Tetra-*O*-benzyl-1-*C*-vinyl-α-D-mannopyranose (3c). Following the procedure of preparing **3a**, 2,3,4,6-tetra-*O*-benzylmannono-1,5-lactone (**1c**) (580 mg, 1.1 mmol) reacted with vinyl magnesium bromide (1.5 equiv.) to provide the compound **3c** (513 mg, 82.4%). Colorless syrup; $[\alpha]_D^{23}$: +10.4° (*c* 1.0, $CHCl_3$); IR (neat): 3383.55, 3063.33, 3032.47, 2918.65, 1604.97, 1496.94, 1454.50, 1365.77, 1275.10, 1209.51, 1072.55, 941.38, 738.83, 698.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.66 (s, br, 1H, OH), 3.72 (d, br, 2H, J=3.66 Hz, two 6-H), 3.74 (d, 1H, J=2.75 Hz, 2-H), 3.93 (t, 1H, J=9.76 Hz, 4-H), 4.02 (dt, 1H, J=10.07 Hz, J=3.66 Hz, 5-H), 5.12 (dd, 1H, J= 9.64 Hz, J=2.75 Hz, 3-H), 4.53–4.63 (m, 4H, CH_2Ph), 4.70 (s, 2H, CH_2Ph), 4.84 (d, 1H, J=12.20 Hz, CH_2Ph), 4.87 (dd, 1H, J=11.29 Hz, CH_2Ph), 5.20 (d, 1H, J= 10.68 Hz, CH_2=), 5.47 (d, 1H, J=17.40 Hz, CH_2=), 6.11 (dd, 1H, J=17.39 Hz, J=10.68 Hz, -CH=), 7.17–7.36 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 69.66 (6-C), 72.37 (5-C), 72.88 (CH_2Ph), 73.28 (CH_2Ph), 74.60 (CH_2Ph), 74.94 (CH_2Ph), 74.97 (2-C), 78.82 (4-C), 81.34 (3-C), 97.30 (1-C), 115.90 (CH_2=), 127.33 (Ph), 127.36 (Ph), 127.46 (Ph), 127.78 (Ph), 127.86 (Ph), 127.97 (Ph), 128.02 (Ph), 128.22 (Ph), 128.30 (Ph), 138.43 (Ph), 138.46 (Ph), 138.52 (Ph), 138.59 (Ph), 140.23 (CH_2=); HRMS (FAB): calcd. for $C_{36}H_{38}O_6Na$ 589.2566, found 589.2573.

3.2. The *O*-glycosidations of the 1-*C*-methyl-hexopyranoses 2

3.2.1. The examination of the reaction conditions using 2a and 4. To a solution of **2a** (55.4 mg, 0.1 mmol), methyl 2,3,4-tri-*O*-benzyl-α-D-glucoside (**4**) (69.6 mg, 0.15 mmol) and MS 4A (100 mg) in dry dichloromethane (2.0 mL) was added the given amount of Lewis acids under argon atmosphere. The mixture was stirred for a certain time, then 3 drops of Et_3N was added to quench the reaction. The solution was concentrated in vacuum, and the residue was submitted to a silica gel column chromatography (Et_2O: Hexane=1:1 v/v) to afford the disaccharide **5a**. The results are summarized in Table 1.

3.2.2. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-methyl-α-D-glucopyranosyl)-(1′→6)-2,3,4-tri-*O*-benzyl-α-D-glucoside (5a). TMSOTf (1.8 μL, 0.02 mmol, 0.2 equiv.) was added to the solution of **2a** (55.4 mg, 0.1 mmol), methyl 2,3,4-tri-*O*-benzyl-α-D-glucoside (**4**) (69.6 mg, 0.15 mmol) and molecular sieves 4A (MS 4A, 100 mg) in dichloromethane (2.0 mL) was added at 0°C under argon atmosphere. The mixture was stirred for 2 h, and the reaction was quenched by Et_3N. The solvent was removed, and the residue was submitted to a silica gel column chromatography using Et_2O: Hexane (1:1 v/v) as the eluent to afford the disaccharide **5a** (90.4 mg, 90.3%). Colorless syrup; $[\alpha]_D^{23}$: +47.7° (*c* 1.0, $CHCl_3$) (lit.[11] +46.9°).

3.2.3. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-methyl-α-D-galactopyranosyl)-(1′→6)-2,3,4-tri-*O*-benzyl-α-D-glucoside (5b). Following the glycosidation procedure of **2a** and **4**, the glycosidation of **2b** (55.4 mg, 0.1 mmol) and **4** (69.6 mg, 0.15 mmol) was carried out and afforded the disaccharide **5b** (89.2 mg, 89.1%). Colorless syrup; $[\alpha]_D^{23}$: +50.8° (*c* 1.0, $CHCl_3$) (lit.[11] +51.3°).

3.2.4. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-methyl-α-D-mannopyranosyl)-(1′→6)-2,3,4-tri-*O*-benzyl-α-D-glucoside (5c). Following the glycosidation procedure of **2a** and **4**, the glycosidation of **2c** (55.4 mg, 0.1 mmol) and **4** (69.6 mg, 0.15 mmol) was carried out and afforded the disaccharide **5c** (86.9 mg, 86.8%). Colorless syrup; $[\alpha]_D^{25}$: +44.0° (*c* 1.0, $CHCl_3$) (lit.[11] +43.1°).

3.3. The *O*-glycosidations of the 1-*C*-vinyl-hexopyranoses 3

3.3.1. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-vinyl-α-D-glucopyranosyl)-(1′→6)-2,3,4-tri-*O*-benzyl-α-D-glucoside (6a). A solution of **3a** (803 mg, 1.42 mmol), **4** (985 mg, 2.12 mmol, 1.5 equiv.) and MS 4A (1.0 g) in 30 mL of dry CH_2Cl_2 was cooled to 0°C under argon atmosphere, and 25.6 μL (0.28 mmol, 0.2 equiv.) of TMSOTf was added. The solution was stirred for 1 h, and 0.1 mL of Et_3N was added to quench the reaction. The solvent was removed, and the residue was applied on a silica gel column chromatography (Et_2O: Hexane=1:1.5 v/v) to give the disaccharide **6a** (1.27 g, 88.3%). Colorless syrup; $[\alpha]_D^{23}$: +40.7° (*c* 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2928.30, 1604.97, 1496.94, 1454.50, 1361.91, 1207.59, 1159.36, 1093.77, 1028.18, 943.31, 910.51, 736.90, 698.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.31–3.37 (m, 3H, 2′-H, 4-H and 6-H), 3.35

(s, 3H, CH_3O), 3.50 (dd, 1H, J=9.76 Hz, J=3.66 Hz, 2-H), 3.60 (dd, 1H, J=11.29 Hz, J=1.53 Hz, 6′-H), 3.63–3.71 (m, 3H, 6′-H, 4′-H and 6-H), 3.81–3.86 (m, 1H, 5-H), 3.87–3.91 (m, 1H, 5′-H), 3.98 (t, 1H, J=9.15 Hz, 3-H), 4.09 (t, 1H, J=9.15 Hz, 3′-H), 4.48–4.68 (m, 7H, CH_2Ph and 1-H), 4.75–4.89 (m, 7H, CH_2Ph), 4.96 (d, 1H, J=10.99 Hz, CH_2Ph), 5.27 (dd, 1H, J=10.69 Hz, J= 1.83 Hz, CH_2=), 5.54 (dd, 1H, J=17.70 Hz, J=1.83 Hz, CH_2=), 5.90 (dd, 1H, J=17.70 Hz, J=10.98 Hz, -CH=), 7.15–7.36 (m, 35H, ArH); ^{13}C NMR ($CDCl_3$): δ 54.94 (OCH_3), 61.45 (6-C), 68.88 (6′-C), 69.93 (5-C), 71.57 (5′-C), 73.20 (two C, CH_2Ph), 74.54 (CH_2Ph), 74.84 (CH_2Ph), 75.18 (CH_2Ph), 75.33 (CH_2Ph), 75.79 (CH_2Ph), 78.39 (4′-C), 78.55 (4-C), 80.16 (2-C), 82.35 (3-C), 82.73 (3′-C), 84.49 (2′-C), 97.51 (1-C), 99.58 (1′-C), 118.94 (CH_2=), 127.37 (Ph), 127.38 (Ph), 127.45 (Ph), 127.49 (Ph), 127,57 (Ph), 127.60 (Ph), 127.79 (Ph), 127.84 (Ph), 127.95 (Ph), 128.01 (Ph), 128.12 (Ph), 128.19 (Ph), 128.27 (Ph), 128.34 (Ph), 128.37 (Ph), 128.40 (Ph), 135.42 (-CH=), 138.22 (Ph), 138.27 (Ph), 138.48 (Ph), 138.54 (Ph), 138.67 (Ph), 138.71 (Ph); HRMS (FAB): calcd for $C_{64}H_{68}O_{11}Na$ 1035.4660, found 1035.4655.

3.3.2. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-vinyl-α-D-galactopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-benzyl-α-D-glucoside (6b). Following the glycosidation procedure of **3a** and **4**, the glycosidation of **3b** (380 mg, 0.67 mmol) and **4** (464 mg, 1.0 mmol, 1.5 equiv.) provided the disaccharide **6b** (482 mg, 71.0%). Colorless syrup; $[\alpha]_D^{23}$: +36.0° (*c* 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2926.37, 1496.94, 1454.50, 1361.91, 1205.66, 1097.63, 1049.40, 1028.18, 943.31, 912.44, 734.97, 698.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.23 (s, 3H, OCH_3), 3.26 (t, 1H, J=9.61 Hz, 4-H), 3.32 (dd, 1H, J=10.68 Hz, J=7.63 Hz, 6′-H), 3.47 (dd, 1H, J=9.46 Hz, J=3.66 Hz, 2-H), 3.53–3.61 (m, 2H, two 6-H), 3.71 (dd, 1H, J =10.68 Hz, J=1.52 Hz, 6′-H), 3.80–3.85 (m, 1H, 5-H), 3.84 (d, 1H, J=9.76 Hz, 2′-H), 3.93 (s, br., 1H, 4′-H), 3.97 (t, 1H, J=9.16 Hz, 3-H), 4.00–4.04 (m, 2H, 5′-H and 3′-H), 4.39–4.48 (m, 3H, CH_2Ph), 4.55 (d, 1H, J=3.66 Hz, 1-H), 4.60–4.97 (m, 11H, CH_2Ph), 5.23 (dd, 1H, J=10.98 Hz, J=1.83 Hz, CH_2=), 5.51 (dd, 1H, J=17.70 Hz, J =1.83 Hz, CH_2=), 5.89 (dd, 1H, J=17.40 Hz, J=10.99 Hz, -CH=), 7.21–7.34 (m, 35H, ArH); ^{13}C NMR ($CDCl_3$): δ 54.65 (OCH_3), 61.58 (6-C), 68.95 (6′-C), 69.90 (5-C), 70.07 (5′-C), 72.40 (CH_2Ph), 73.04 (CH_2Ph), 73.10 (CH_2Ph), 74.39 (CH_2Ph), 74.83 (4′-C), 75.08 (CH_2Ph), 75.15 (CH_2Ph), 75.67 (CH_2Ph), 78.83 (4-C), 79.62 (3′-C), 80.05 (2-C), 80.51 (2′-C), 82.20 (3-C), 97.38 (1-C), 99.90 (1′-C), 118.82 (CH_2=), 127.22 (Ph), 127.33 (Ph), 127.35 (Ph), 127.39 (Ph), 127.42 (Ph), 127.48 (Ph), 127.53 (Ph), 127.59 (Ph), 127.63 (Ph), 127.74 (Ph), 127.79 (Ph), 127.83 (Ph), 127.90 (Ph), 128.00 (Ph), 128.09 (Ph), 128.13 (Ph), 128.25 (Ph), 128.28 (Ph), 128.33 (Ph), 135.18 (-CH=), 138.16 (Ph), 138.28 (Ph), 138.62 (Ph), 138.70 (Ph), 138.73 (Ph), 138.97 (Ph); HRMS (FAB): calcd for $C_{64}H_{68}O_{13}Na$ 1035.4660, found 1035.4663.

3.3.3. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-vinyl-α-D-mannopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-benzyl-α-D-glucoside (6c). Following the glycosidation procedure of **3a** and **4**, the glycosidation of **3c** (504 mg, 0.89 mmol) and **4** (600 mg, 1.29 mmol, 1.45 equiv.) provided the disaccharide **6c** (702 mg, 78.0%). Colorless syrup; $[\alpha]_D^{23}$: +30.9° (*c* 1.3, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2910.94, 1603.04, 1496.94, 1454.50, 1361.91, 1275.10, 1205.66, 1095.70, 1028.18, 910.51, 827.56, 736.90, 698.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.30 (s, 3H, CH_3O), 3.28–3.35 (m, 1H, 4-H, overlapped with OCH_3), 3.46 (dd, 1H, J=11.00 Hz, J=6.05 Hz, 6-H), 3.54 (dd, 1H, J=9.90 Hz, J=3.85 Hz, 2-H), 3.66 (dd, 1H, J=11.54 Hz, J=1.65 Hz, 6′-H), 3.68 (dd, 1H, J=10.45 Hz, J=1.65 Hz, 6-H), 3.72 (dd, 1H, J=11.54 Hz, J=4.95 Hz, 6′-H), 3.72–3.75 (m, 1H, 5-H), 3.78 (ddd, 1H, J=9.90 Hz, J=5.50 Hz, J=4.40 Hz, 5′-H), 3.82 (d, 1H, J=2.75 Hz, 2′-H), 3.97 (t, 2H, J=9.35 Hz, 4′-H and 3-H), 4.09 (dd, 1H, J=9.35 Hz, J=2.75 Hz, 3′-H), 4.44–4.55 (m, 3H, CH_2Ph and 1-H), 4.60–4.71 (m, 6H, CH_2Ph), 4.75–4.90 (m, 5H, CH_2Ph), 4.98 (d, 1H, J= 10.68 Hz, CH_2Ph), 5.35 (dd, 1H, J=10.38 Hz, J=1.83 Hz, CH_2=), 5.54 (dd, 1H, J=17.40 Hz, J=1.84 Hz, CH_2=), 5.65 (dd, 1H, J=17.40 Hz, J=10.38 Hz, -CH=), 7.14–7.37 (m, 35H, ArH); ^{13}C NMR ($CDCl_3$): δ 54.86 (OCH_3), 60.52 (6-C), 69.37 (6′-C), 69.64 (5-C), 71.91 (CH_2Ph), 73.08 (CH_2Ph), 73.11 (two C, 5′-C and CH_2Ph, overlapped), 74.62 (two C, 4′-C and CH_2Ph, overlapped), 74.71 (CH_2Ph), 74.75 (CH_2Ph), 75.70 (CH_2Ph), 78.02 (4-C), 78.16 (2′-C), 79.93 (2-C), 80.65 (3′-C), 82.35 (3-C), 97.57 (1-C), 100.50 (1′-C), 119.26 (CH_2=), 127.20 (Ph), 127.23 (Ph), 127.27 (Ph), 127.43 (Ph), 127.45 (Ph), 127.49 (Ph), 127.55 (Ph), 127.59 (Ph), 127.66 (Ph), 127.81 (Ph), 127.84 (Ph), 127.93 (Ph), 127.96 (Ph), 127.98 (Ph), 128.08 (Ph), 128.11 (Ph), 128.13 (Ph), 128.22 (Ph), 128.32 (Ph), 128.39 (Ph), 135.84 (-CH=), 138.16 (Ph), 138.20 (Ph), 138.43 (Ph), 138.67 (Ph), 138.69 (Ph), 138.79 (Ph), 138.81 (Ph); HRMS (FAB): calcd for $C_{64}H_{68}O_{11}Na$ 1035.4660, found 1045.4667.

3.3.4. Methyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-α-D-glucopyranoside (7a). To a mixture of 2.22 g (4.0 mmol) of **2a**, 0.8 mL (20 mmol) of dry methanol and 2.0 g of anhydrous magnesium sulfate ($MgSO_4$) in 20 mL of dry CH_2Cl_2 was added 72 μL of TMSOTf (0.2 equiv.) at 0°C under argon atmosphere. The solution was stirred at 0°C for 1 h and 0.1 mL of Et_3N was added to quench the reaction. After removing the solvent, the residue was applied on a silica gel column chromatography using AcOEt: Hexane=1:1.5 (v/v) as the eluent to afford the product **7a**, 2.08 g (91.5%). Colorless syrup; $[\alpha]_D^{23}$: +21.3° (*c* 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2910.94, 2866.57, 1496.94, 1454.50, 1361.91, 1211.44, 1089.91, 1028.18, 736.90, 689.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, CH_3), 3.22 (s, 3H, OCH_3), 3.35 (d, 1H, J=9.46 Hz, 2-H), 3.63–3.72 (m, 4H, two 6-H, 3-H and 4-H), 4.25–4.11 (m, 1H, 5-H), 4.50–4.54 (m, 2H, CH_2Ph), 4.61 (d, 1H, J=12.21 Hz, CH_2Ph), 4.69 (d, 1H, J=11.29 Hz, CH_2Ph), 4.82–4.94 (m, 4H, CH_2Ph), 7.14–7.16 (m, 2H, ArH), 7.257.32 (m, 18H, ArH); ^{13}C NMR ($CDCl_3$): δ 19.91 (CH_3), 47.85 (OCH_3), 68.76 (6-C), 71.47 (5-C), 73.33 (CH_2Ph), 74.87 (CH_2Ph), 75.49 (CH_2Ph), 75.64 (CH_2Ph), 78.57 (4-C), 83.29 (3-C), 83.79 (2-C), 100.26 (1-C), 127.47 (Ph), 127.50 (Ph), 127.58 (Ph), 127.66 (Ph), 127.70 (Ph), 127.77 (Ph), 128.23 (Ph), 128.25 (Ph), 128.28 (Ph), 128.33 (Ph), 128.71 (Ph), 137.93 (Ph), 138.15 (Ph), 138.18 (Ph), 138.70 (Ph); HRMS (FAB): calcd for $C_{36}H_{40}O_6Na$ 591.2723, found 591.2715.

3.3.5. Methyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-α-D-galactopyranoside (7b). Following the procedure of

preparing **7a**, the compound **7b** (1.62 g, 95.1%) was obtained from 1.66 g (3.0 mmol) of **2b**. Colorless syrup; $[\alpha]_D^{23}$: +15.3° (*c* 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2916.72, 2868.50, 1604.97, 1585.68, 1496.94, 1454.50, 1363.84, 1197.94, 1095.70, 1049.40, 916.30, 734.97, 698.32 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.28 (s, 3H, CH_3), 3.20 (s, 3H, OCH_3), 3.50–3.60 (m, 2H, two 6-H), 3.74–3.78 (m, 1H, 5-H), 3.85 (d, 1H, *J*=10.07 Hz, 2-H), 3.97 (s, br, 1H, 4-H), 4.02 (d, 1H, *J*=9.77 Hz, 3-H), 4.41 (d, 1H, *J*=11.90 Hz, CH_2Ph), 4.49 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.60 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.71 (d, 1H, *J*=11.30 Hz, CH_2Ph), 4.73 (s, br, 2H, CH_2Ph), 4.92–4.96 (m, 2H, CH_2Ph), 7.24–7.38 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 20.09 (CH_3), 48.14 (OCH_3), 69.10 (6-C), 70.21 (5-C), 72.79 (CH_2Ph), 73.49 (4-C), 74.54 (CH_2Ph), 74.96 (CH_2Ph), 75.72 (CH_2Ph), 80.26 (2-C), 80.60 (3-C), 100.73 (1-C), 127.49 (Ph), 127.67 (Ph), 127.76 (Ph), 128.12 (Ph), 128.16 (Ph), 128.21 (Ph), 128.37 (Ph), 138.06 (Ph), 138.26 (Ph), 138.71 (Ph), 138.89 (Ph); HRMS (FAB): calcd for $C_{36}H_{40}O_6Na$ 591.2723, found 591.2720.

3.3.6. Methyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-α-D-mannopyranoside (7c). Following the procedure of preparing **7a**, the compound **7c** (2.10 g, 92.4%) was obtained from 2.22 g (4.0 mmol) of **2c**. Colorless syrup; $[\alpha]_D^{23}$: +28.8° (*c* 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2912.65, 2866.52, 1604.97, 1496.94, 1454.50, 1363.23, 1198.56, 1095.70 1049.40, 915.86, 735.82, 698.32 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.34 (s, 3H, CH_3), 3.20 (s, 3H, OCH_3), 3.60–3.64 (m, 1H, 5-H), 3.68 (d, 1H, *J*=2.75 Hz, 2-H), 3.73–3.74 (m, 2H, two 6-H), 3.91 (t, 1H, *J*=9.46 Hz, 4-H), 4.12 (dd, 1H, *J*=9.16 Hz, *J*=2.75 Hz, 3-H), 4.52 (d, 1H, *J*=10.99 Hz, CH_2Ph), 4.56 (d, 1H, *J*=12.60 Hz, CH_2Ph), 4.65 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.66 (d, 1H, *J*=11.60 Hz, CH_2Ph), 4.74 (d, 2H, *J*=2.44 Hz, CH_2Ph), 4.85 (d, 1H, *J*=10.99 Hz, CH_2Ph), 4.97 (d, 1H, *J*=11.59 Hz, CH_2Ph), 7.15–7.38 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$): δ 19.24 (CH_3), 47.64 (OCH_3), 69.48 (6-C), 72.48 5-C), 72.98 (CH_2Ph), 73.23 (CH_2Ph), 74.80 (CH_2Ph), 74.87 (CH_2Ph), 74.92 (2-C), 78.29 (4-C), 81.65 (3-C), 101.14 (1-C), 127.28 (Ph), 127.39 (Ph), 127.41 (Ph), 127.46 (Ph), 127.66 (Ph), 127.94 (Ph), 128.00 (Ph), 128.11 (Ph), 128.17 (Ph), 128.22 (Ph), 128.30 (Ph), 138.45 (Ph), 138.55 (Ph), 138.59 (Ph), 138.69 (Ph); HRMS (FAB): calcd for $C_{36}H_{40}O_6Na$ 591.2723, found 591.2724.

3.3.7. Methyl 2,3,4,6-tetra-*O*-acetyl-1-*C*-methyl-α-D-glucopyranoside (8a). A mixture of 738 mg (1.33 mmol) of **7a**, 200 mg of $Pd(OH)_2/C$ (20 wt%) and 26 mL of anhydrous methanol was stirred vigorously under atmospheric pressure of H_2 at room temperature until the starting material disappeared (TLC: CH_2Cl_2/CH_3OH=10:1). The catalyst was filtered out and the solvent was removed under reduced pressure and dried in vacuum overnight to afford debenzylated product quantitatively. The crude product (257 mg 1.24 mmol) was dissolved in 9.0 mL of dry pyridine and 4.0 mL of acetic anhydride. The solution was stirred under argon atmosphere at room temperature overnight, then poured into 200 g of ice-water. The mixture was extracted with AcOEt (50 mL×3). The organic solution was washed with water (50 mL×5), dried over Na_2SO_4 and concentrated in vacuum. The residue was applied on a silica gel column chromatography using AcOEt: Hexane (1:1.5) as the eluent to yield the acetylated product **8a** (411 mg, 88.2%). White solid, mp. 74–76°C; $[\alpha]_D^{25}$: +91.7° (*c* 1.0, $CHCl_3$); IR (KBr): 2997.74, 2964.95, 2839.56, 1747.72, 1435.21, 1371.55, 1240.38, 1122.71, 1037.83, 985.74, 908.58, 868.07 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.35 (s, 3H, CH_3), 1.98 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 3.28 (s, 3H, OCH_3), 3.86 (dq, 1H, *J*=10.07 Hz, *J*=2.44 Hz, 5-H), 4.09 (dd, 1H, *J*=12.51 Hz, *J*=2.44 Hz, 6-H), 4.24 (dd, 1H, *J*=12.21 Hz, *J*=4.89 Hz, 6-H), 5.01 (d, 1H, *J*=10.07 Hz, 2-H), 5.08 (t, 1H, *J*=9.77 Hz, 4-H), 5.47 (t, 1H, *J*=9.62 Hz, 3-H); ^{13}C NMR ($CDCl_3$): δ 19.42 (1-CH_3), 20.58 (two C, CH_3), 20.67 (CH_3), 20.71 (CH_3), 48.22 (CH_3O), 62.18 (6-C), 68.41 (5-C), 68.87 (4-C), 71.15 (3-C), 73.57 (2-C), 99.46 (1-C), 169.53 (C=O), 169.96 (C=O), 170.10 (C=O), 170.65 (C=O); HRMS (FAB): calcd for $C_{16}H_{24}O_{10}Na$ 399.1268, found 399.1275.

3.3.8. Methyl 2,3,4,6-tetra-*O*-acetyl-1-*C*-methyl-α-D-galactopyranoside (8b). 7b (1.14 g, 2.0 mmol) was debenzylated and then acetylated as described in the preparation of **8a** to give **8b** (640 mg, 85.1%). White solid, mp. 157–159°C; $[\alpha]_D^{23}$: +103.6° (*c* 1.0, $CHCl_3$); IR (KBr): 2982.31, 2949.52, 1749.65, 1450.65, 1435.21, 1377.34, 1223.02, 1143.93, 1115.00, 1086.06, 1060.98, 1043.62, 962.60, 900.87, 846.85 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.37 (s, 3H, CH_3), 1.96 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.16 (s, 3H, CH_3CO), 3.28 (s, 3H, CH_3O), 4.04–4.08 (m, 1H, 5-H), 4.10–4.12 (m, 2H, two 6-H), 5.26 (d, 1H, *J*=10.69 Hz, 2-H), 5.34 (dd, 1H, *J*=10.68 Hz, *J*=3.36 Hz, 3-H), 5.45 (dd, 1H, *J*=3.36 Hz, *J*=1.22 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 19.65 (1-CH_3), 20.55 (CH_3), 20.65 (two C, CH_3), 20.78 (CH_3), 48.31 (OCH_3), 61.82 (6-C), 67.33 (5-C), 68.24 (4-C), 68.62 (3-C), 71.13 (2-C), 99.91 (C-1), 169.99 (C=O), 170.19 (C=O), 170.26 (C=O), 170.39 (C=O); HRMS (FAB): calcd for $C_{16}H_{24}O_{10}Na$ 399.1268, found 399.1266.

3.3.9. Methyl 2,3,4,6-tetra-*O*-acetyl-1-*C*-methyl-α-D-mannopyranoside (8c). 7c (1.14 g, 2.0 mmol) was debenzylated and then acetylated as described in the preparation of **8a** to give **8c** (658 mg, 87.5%). White solid, mp. 95–96°C; $[\alpha]_D^{25}$: +65.9° (*c* 1.0, $CHCl_3$); IR (KBr): 2970.74, 2910.94 2839.56, 1747.72, 1435.21, 1371.55, 1224.95, 1124.64, 1086.06, 1057.12, 991.53, 958.74, 906.65, 862.29 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.29 (s, 3H, CH_3), 1.96 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.17 (s, 3H, CH_3CO), 3.23 (s, 3H, OCH_3), 3.80–3.86 (m, 1H, 5-H), 4.10–4.26 (m, 2H, two 6-H), 5.20 (t, 1H, *J*=10.07 Hz, 4-H), 5.23 (d, 1H, *J*=3.05 Hz, 2-H), 5.44 (dd, 1H, *J*=10.06 Hz, *J*=3.06 Hz, 3-H); ^{13}C NMR ($CDCl_3$): δ 18.36 (1-CH_3), 20.62 (CH_3), 20.70 (CH_3), 20.73 (CH_3), 20.76 (CH_3), 48.11 (CH_3O), 62.90 (6-C), 66.07 (5-C), 69.38 (4-C), 69.87 (2-C), 71.48 (3-C), 100.06 (1-C), 169.81 (C=O), 169.90 (C=O), 170.01 (C=O), 170.64 (C=O); HRMS (FAB): calcd for $C_{16}H_{24}O_{10}Na$ 399.1268, found 399.1271.

3.4. The *O*-transglycosidations of the methyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-hexopyranosides 7

3.4.1. The examination of the reaction conditions using 7a and 4. To a solution of **7a** (114 mg, 0.2 mmol), methyl

2,3,4-tri-*O*-benzyl-α-D-glucoside (**4**) (140 mg, 0.3 mmol, 1.5 equiv.) and MS 4A (500 mg) in dry dichloromethane (5.0 mL) was added a certain amount of Lewis acids under argon atmosphere. The mixture was stirred for the given time, then 0.1 mL of Et_3N was added to quench the reaction. After removing the solvent, the residue was submitted to a silica gel column chromatography (Et_2O: Hexane=1:1 v/v) to afford the disaccharide **5a**. The results are listed in Table 2.

3.4.2. The *O*-transglycosidation of the methyl 2,3,4,6-tetra-*O*-bezyl-1-*C*-methyl-α-D-glucopyranoside 7a. To a solution of **7a** (114 mg, 0.2 mmol), methyl 2,3,4-tri-*O*-benzyl-α-D-glucoside (**4**) (140 mg, 0.3 mmol, 1.5 equiv.) and MS 4A (500 mg) in dry dichloromethane (5.0 mL) was added $SnCl_4$ (23 μL, 0.2 mmol, 1.0 equiv.) at 0°C under argon atmosphere. The mixture was stirred for 3 h at 0°C, then 0.1 mL of Et_3N was added to quench the reaction. The solvent was removed, and the residue was submitted to a silica gel column chromatography using Et_2O: Hexane (1:1 v/v) as the eluent to afford the disaccharide **5a** (161.4 mg, 80.6%) with the recovery of **7a** (7.8 mg, 6.8%). **5a**: colorless syrup; $[\alpha]_D^{23}$: +46.1° (*c* 1.0, $CHCl_3$) (lit.[11] +46.9°).

3.4.3. The *O*-transglycosidation of the methyl 2,3,4,6-tetra-*O*-bezyl-1-*C*-methyl-α-D-galactopyranoside 7b. The reaction of **7b** (114 mg, 0.2 mmol) and **4** (140 mg, 0.3 mmol, 1.5 equiv.) was carried out following the procedure of the *O*-transglycosidation of **7a**, and the disaccharide **5b** (156.4 mg, 78.1%) was obtained as colorless syrup with the recovery of **7b** (9.8 mg, 8.6%). **5b**: $[\alpha]_D^{23}$: +52.4° (*c* 1.0, $CHCl_3$) (lit.[11] +51.3°).

3.4.4. The *O*-transglycosidation of the methyl 2,3,4,6-tetra-*O*-bezyl-1-*C*-methyl-α-D-mannopyranoside 7c. The reaction of **7c** (114 mg, 0.2 mmol) and **4** (140 mg, 0.3 mmol, 1.5 equiv.) was carried out following the procedure of the *O*-transglycosidation of **7a**, and the disaccharide **5c** (169.8 mg, 84.8%) was obtained as colorless syrup with the recovery of **7c** (7.4 mg, 6.4%). **5c**: $[\alpha]_D^{23}$: +42.0° (*c* 1.0, $CHCl_3$) (lit.[11] +43.1°).

3.5. The *O*-transglycosidations of methyl 2,3,4,6-tetra-*O*-acetyl-1-*C*-methyl-hexopyranosides 8

3.5.1. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-acetyl-1′-*C*-methyl-α-D-glucopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-acetyl-α-D-glucoside (11a). To a solution of **8a** (38 mg, 0.1 mmol), methyl 2,3,4-tri-*O*-acetyl-α-D-glucoside (**10**) (64 mg, 0.2 mmol) and MS 4A (100 mg) in dry CH_2Cl_2 (2 mL) was added $SnCl_4$ (46.7 μL, 0.4 mmol, 4.0 equiv.) under argon atmosphere at 0°C. The mixture was stirred for 2 h at 0°C, and 1 h at room temperature, then 0.1 mL of Et_3N was added to quench the reaction. The solvents were removed, and the residue was applied on a silica gel column chromatography (AcOEt: Hexane=1.5:1) to afford the disaccharide 11a (20.0 mg, 30.1%). Colorless syrup; $[\alpha]_D$: +116.5° (*c* 1.0, $CHCl_3$) (lit.[11] +118.7°).

3.5.2. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-acetyl-1′-*C*-methyl-α-D-galactopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-acetyl-α-D-glucoside (11b). Following the reaction procedure of **8a** and **10**, the transglycosidation of **8b** (38 mg, 0.1 mmol) afforded the disaccharide **11b** (41.8 mg, 63.0%). Colorless syrup; $[\alpha]_D^{25}$: +138.2° (*c* 1.0, $CHCl_3$) (lit.[11] +140.7°).

3.5.3. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-acetyl-1′-*C*-methyl-α-D-mannopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-acetyl-α-D-glucoside (11c). Following the reaction procedure of **8a** and **10**, the transglycosidation of **8c** (38 mg, 0.1 mmol) afforded the disaccharide **11c** (55.0 mg, 82.8%). Colorless syrup; $[\alpha]_D^{24}$: +104.8° (*c* 1.0, $CHCl_3$) (lit.[11] +102.6°).

3.5.4. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-methoxycarbonyl-α-D-glucopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-benzyl-α-D-glucoside (12a). 5.0 mL of a methanolic NaOH solution (2.5 mol/L, 10.0 equiv.) was added to a solution of 1.27 g (1.25 mmol) of **6a** in 20 mL of dry CH_2Cl_2 at −78°C with stirring, and ozone was passed through the solution for 4 h. The reaction mixture was diluted with ether and water, allowed to warm to room temperature and extracted with ether. The organic phase was washed with water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was submitted to a silica gel column chromatography (Et_2O: Hexane 1:1) to afford the product **12a** (425 mg, 32.5%). Colorless syrup; $[\alpha]_D^{23}$: +33.4 (*c* 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2926.37, 1755.44, 1496.94, 1454.50, 1361.91, 1273.17, 1209.51, 1049.40, 910.51, 738.83, 698.32 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.21 (dd, 1H, *J*=10.38 Hz, *J*=8.85 Hz, 4-H), 3.38 (s, 3H, CH_3O), 3.49 (dd, 1H, *J*=9.46 Hz, *J*=3.36 Hz, 2-H), 3.52 (s, 3H, CH_3OCO), 3.54 (dd, 1H, *J*=9.77 Hz, *J*=8.24 Hz, 6-H), 3.60 (dd, 1H, *J*=12.60 Hz, *J*=1.84 Hz, 6′-H), 3.67 (dd, 1H, *J*=11.29 Hz, *J*=3.97 Hz, 6′-H), 3.68 (t, 1H, *J*=9.15 Hz, 4′-H), 3.82 (d, 1H, *J*=9.46 Hz, 2′-H), 4.01 (t, 1H, *J*=9.16 Hz, 3-H), 4.05 (t, 1H, *J*=9.16 Hz, 3′-H), 4.04–4.09 (m, 2H, 5-H and 5′-H), 4.21 (dd, 1H, *J*=10.37 Hz, *J*=1.22 Hz, 6-H), 4.46 (d, 1H, *J*=12.21 Hz, CH_2Ph), 4.52–4.61 (m, 5H, CH_2Ph and 1-H), 4.65 (d, 1H, *J*=12.21 Hz, CH_2Ph), 4.73–4.87 (m, 7H, CH_2Ph), 4.96 (d, 1H, *J*=10.69 Hz, CH_2Ph), 7.13–7.34 (m, 35H, ArH); ^{13}C NMR ($CDCl_3$): δ 52.22 (CH_3OCO), 55.02 (OCH_3), 63.58 (6-C), 68.41 (6′-C), 69.84 (5-C), 72.56 (5′-C), 73.06 (CH_2Ph), 73.08 (CH_2Ph), 74.57 (two C, CH_2Ph), 74.70 (CH_2Ph), 75.31 (CH_2Ph), 75.68 (CH_2Ph), 77.92 (4′-C), 78.80 (4-C), 80.01 (2-C), 81.39 (2′-C), 82.19 (3-C), 82.45 (3′-C), 97.35 (1-C), 99.16 (1′C), 127.40 (Ph), 127.46 (Ph), 127.50 (Ph), 127.59 (Ph), 127.67 (Ph), 127.69 (Ph), 127.73 (Ph), 127.90 (Ph), 128.09 (Ph), 128.12 (Ph), 128.20 (Ph), 128.22 (Ph), 128.27 (Ph), 128.33 (Ph), 137.94 (Ph), 138.13 (Ph), 138.18 (Ph), 138.28 (Ph), 138.34 (Ph), 138.41 (Ph), 138.69 (Ph), 167.66 (-COO-); HRMS (FAB): calcd $C_{64}H_{68}O_{13}Na$ 1067.4558, found 1067.4560.

3.5.5. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-methoxycarbonyl-α-D-galactopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-benzyl-α-D-glucoside (12b). Following the ozonolysis procedure of **6a**, the compound **6b** (280 mg, 0.276 mmol) was oxidized to afford the compound **12b** (87.0 mg, 30.2%). Colorless syrup; $[\alpha]_D^{23}$: +35.1° (*c* 1.85, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2916.72, 1753.51, 1496.94, 1454.50, 1361.91, 1271.24, 1093.77, 912.44, 738.83, 698.32 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.15 (t, 1H, *J*=10.07 Hz, 4-H), 3.20 (s, 3H, OCH_3), 3.45 (dd, 1H, *J*=10.77 Hz, *J*=3.36 Hz, 2-H), 3.49 (s, 3H, CH_3OCO), 3.51–3.60 (m, 3H, 6-H and two

6′-H), 3.95–4.04 (m, 4H, 4′-H, 3′-H, 3-H and 5-H), 4.11 (t, br, 1H, J=6.10 Hz, 5′-H), 4.18 (d, br, 1H, J=9.15 Hz, 6-H), 4.33 (d, 1H, J=9.77 Hz, 2′-H), 4.38 (d, 1H, J=12.21 Hz, CH_2Ph), 4.44 (d, 1H, J=11.90 Hz, CH_2Ph), 4.48 (d, 1H, J=11.30 Hz, CH_2Ph), 4.53 (d, 1H, J=3.66 Hz, 1-H), 4.61–4.84 (m, 9H, CH_2Ph), 4.94 (d, 1H, J=10.68 Hz, CH_2Ph), 4.96 (d, 1H, J=11.60 Hz, CH_2Ph), 7.21–7.33 (m, 35H, ArH); ^{13}C NMR ($CDCl_3$): δ 52.26 (CH_3OCO), 54.73 (CH_3O), 63.68 (6-C), 68.55 (6′-C), 69.75 (5-C), 71.28 (5′-C), 72.42 (CH_2Ph), 73.08 (CH_2Ph), 73.12 (CH_2Ph), 74.40 (CH_2Ph), 74.63 (two C, 4′-C and CH_2Ph), 74.81 (CH_2Ph), 75.69 (CH_2Ph), 77.30 (2′-C), 79.12 (4-C), 79.62 (3-C), 79.95 (2-C), 82.13 (3′-C), 97.35 (1-C), 99.68 (1′-C), 127.26 (Ph), 127.47 (Ph), 127.49 (Ph), 127.51 (Ph), 127.61 (Ph), 127.67 (Ph), 127.78 (Ph), 127.92 (Ph), 128.04 (Ph), 128.14 (Ph), 128.23 (Ph), 128.32 (Ph), 128.35 (Ph), 128.37 (Ph), 128.42 (Ph), 138.14 (Ph), 138.16 (Ph), 138.38 (Ph), 138.76 (Ph), 167.47 (-COO-); HRMS (FAB): calcd for $C_{64}H_{68}O_{13}Na$ 1067.4558, found 1067.4556.

3.5.6. Methyl *O*-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-*C*-methoxycarbonyl-α-D-mannopyranosyl)-(*1′→6*)-2,3,4-tri-*O*-benzyl-α-D-glucoside (12c). Following the ozonolysis procedure of **6a**, the compound **6c** (540 mg, 0.53 mmol) was oxidized to afford the compound 12c (172 mg, 31.1%). Colorless syrup; $[\alpha]_D^{23}$: +33.3° (c 1.0, $CHCl_3$); IR (neat): 3063.33, 3030.54, 2920.66, 1751.86, 1496.94, 1454.50, 1361.91, 1272.36, 1199.98, 1056.12, 911.58, 738.83, 698.32 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.31 (s, 3H, OCH_3), 3.32–3.35 (m, 2H, 4-H and 6-H), 3.47–3.53 (m, 2H, 2-H and 6′-H), 3.59 (s, 3H, CH_3OCO-), 3.69–3.83 (m, 5H, 6′-H, 5-H, 5′-H, 2′-H and 6-H), 3.97–4.06 (m, 3H, 3′-H, 4′-H and 3-H), 4.46–4.63 (m, 5H, CH_2Ph and 1-H), 4.67–4.71 (m, 3H, CH_2Ph), 4.76–4.80 (m, 3H, CH_2Ph), 4.87–4.91 (m, 2H, CH_2Ph), 4.96–5.01 (m, 2H, CH_2Ph), 7.14–7.34 (m, 35H, ArH); ^{13}C NMR ($CDCl_3$): δ 52.25 (CH_3OCO), 55.08 (CH_3O), 62.86 (6-C), 68.59 (6′-C), 69.25 (5-C), 72.25 (CH_2Ph), 73.16 (5′-C), 73.23 (CH_2Ph), 73.84 (CH_2Ph), 74.41 (CH_2Ph), 74.53 (CH_2Ph), 74.62 (4′-C), 74.95 (CH_2Ph), 75.70 (CH_2Ph), 76.68 (2′-C), 77.51 (4-C), 79.86 (2-C), 80.33 (3′-C), 82.20 (3-C), 97.67 (1-C), 99.23 (1′-C), 127.37 (Ph), 127.45 (Ph), 127.47 (Ph), 127.52 (Ph), 127.59 (Ph), 127.62 (Ph), 127.67 (Ph), 127.74 (Ph), 127.78 (Ph), 127.82 (Ph), 127. 88 (Ph), 127.98 (Ph), 128.12 (Ph), 128.138 (Ph), 128.22 (Ph), 128.30 (Ph), 128.34 (Ph), 128.43 (Ph), 137.90 (Ph), 137.92 (Ph), 138.10 (Ph), 138.42 (Ph), 138.66 (Ph), 167.31 (-COO-); HRMS (FAB): calcd for $C_{64}H_{68}O_{13}Na$ 1067.4558, found 1067.4563.

Acknowledgements

We are grateful to Miss J. Shimode and Miss M. Kitsukawa for spectroscopic measurements. Partial financial support for this research from the Ministry of Education, Science, Sports and Culture of Japan is gratefully acknowledged. X. L. thanks the JSPS for a postdoctoral fellowship.

References

1. (a) Ganem, B. *Acc. Chem. Res.* **1996**, *29*, 340–347. (b) Sears, P.; Wong, C. H. *Angew. Chem. Int. Eng.* **1999**, *38*, 2300–2324. (c) Davis, A. P.; Wareham, R. S. *Angew. Chem. Int. Eng.* **1999**, *38*, 2978–2996. (d) St. Hilaire, P. M.; Meldal, M. *Angew. Chem. Int. Eng.* **2000**, *39*, 1162–1179. (e) Davis, B. G. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3215–3237. (f) Danishefsky, S. J.; Allen, J. R. *Angew. Chem. Int. Eng.* **2000**, *39*, 836–863. (g) Vankar, Y. D.; Schmidt, R. R. *Chem. Soc. Rev.* **2000**, *29*, 201–216. (h) Driguez, H.; Thiem, J. *Glycosience, Synthesis of Substrate Analogs and Mimetics*; Springer: Berlin, 1999.
2. (a) Schmidt, R. R.; Castro-Palomino, J. C.; Retz, O. *Pure Appl. Chem.* **1999**, *71*, 729–744. (b) Boons, G.-J. *Carbohydrate Chemistry*; Blackie Academic and Professional: London, 1998. (c) Driguez, H.; Thiem, J. *Glycosience, Synthesis of Oligosaccharides and Glycoconjugates*; Springer: Berlin, 1999. (d) Hanessian, S. *Preparative Carbohydrate Chemistry*; Macel Dekker, Inc.: New York, 1997.
3. (a) Schmidt, R. R. *Pure App. Chem.* **1989**, *61*, 1257–1270. (b) Schmidt, R. R. *Pure App. Chem.* **1998**, *70*, 397–402. (c) Mukaiyama, T.; Murai, Y.; Shoda, S. *Chem. Lett.* **1981**, 431–432. (d) Kunz, H. *Pure App. Chem.* **1993**, *65*, 1223–1232.
4. (a) Schmidt, R. R.; Kinzy, W. Anomeric-oxygen activation for glycoside synthesis: the trichloroacetimidate method. In *Adv. Carbohydr. Chem. Biochem.*; Horton, D., Ed.; Academic Press: San Diego, 1994; Vol. 50, pp 21–123. (b) Wang, Y. L.; Mao, J. M.; Cai, M. S. *Synth. Comm.* **1999**, *29*, 2093–2097.
5. (a) Veeneman, G. H.; van Boon, J. H. *Tetrahedron Lett.* **1990**, *31*, 275–278. (b) Veeneman, G. H.; van Leeuwen, S. H.; van Boon, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331–1334. (c) Garegg, P. J. Thioglycosides as glycosyl donors in oligosaccharide synthesis. In *Adv. Carbohydr. Chem. Biochem.*; Horton, D., Ed.; Academic Press: San Diego, 1997; Vol. 52, pp 179–205.
6. (a) Sabesan, S.; Neira, S. *Carbohydr. Res.* **1992**, *223*, 169–185. (b) Hashimoto, S.; Umeo, K.; Sano, A.; Watanabe, N.; Nakajima, M.; Ikegami, S. *Tetrahedron Lett.* **1995**, *36*, 2251–2254. (c) Hashimoto, S.; Sakamoto, H.; Honda, T.; Ikegami, S. *Tetrahedron Lett.* **1997**, *38*, 5181–5184. (d) Hashimoto, S.; Sakamoto, H.; Honda, T.; Abe, H.; Nakajima, M.; Ikegami, S. *Tetrahedron Lett.* **1997**, *38*, 8969–8972. (e) Plante, O. J.; Andrade, R. B.; Seeberger, P. H. *Org. Lett.* **1999**, *1*, 211–214.
7. (a) Brrown, D. S.; Ley, S. V.; Vile, S. *Tetrahedron Lett.* **1988**, *29*, 4873–4876. (b) Kahne, D.; Walker, S.; Cheng, Y.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 6881–6882. (c) Raghavan, S.; Kahne, D. *J. Am. Chem. Soc.* **1993**, *115*, 1580–1581.
8. (a) Mootoo, D. R.; Date, V.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 2662–2663. (b) Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *Synlett* **1992**, 927–942.
9. (a) Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6656–6660. (b) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661–6666. (c) Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1380–1419. (d) Bussolo, V. D.; Kim, Y. J.; Gin, D. Y. *J. Am. Chem. Soc.* **1998**, *120*, 13515–13516. (e) Bussolo, V. D.; Liu, J.; Hujjman, Jr, L. G.; Gin, D. Y. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 204–207.
10. (a) Inanaga, J.; Yokoyama, Y.; Hanamoto, T. *J. Chem. Soc., Chem. Commn.* **1993**, 1090–1091. (b) Mukaiyama, T.; Matsubara, K.; Hora, M. *Synthesis* **1994**, 1368–1373.

(c) Susaki, H. *Chem. Pharm. Bull.* **1994**, *42*, 1917–1918. (d) Garcia, B. A.; Poole, J. L.; Gin, D. Y. *J. Am. Chem. Soc.* **1997**, *119*, 7597–7598.
11. Li, X. L.; Ohtake, H.; Takahashi, H.; Ikegami, S. *Tetrahedron* **2001**, in press.
12. (a) Heskamp, B. M.; Noort, D.; van der Marel, G. A.; van Boom, J. H. *Synlett* **1992**, 713–715. (b) Heskamp, B. M.; Veeneman, G. H.; van der Marel, G. A.; van Boeckel, C. A. A.; van Boom, J. H. *Tetrahedron* **1995**, *51*, 5657–5670. (c) Dondoni, A.; Marra, A.; Rojo, I.; Scherrmann, M. C. *Tetrahedron* **1996**, *52*, 3057–3074. (d) Dondoni, A.; Marra, A. *Chem. Commun.* **1999**, 2133–2145.
13. Lederkremer, R. M.; Varela, O. Synthetic reactions of aldonolactones. In *Adv. Carbohydr. Chem. Biochem.*; Horton, D., Ed.; Academic Press: San Diego, 1994; Vol. 50, pp 125–209.
14. (a) Csuk, R.; Glanzer, B. I. *J. Carbohydr. Chem.* **1990**, *9*, 797–807. (b) Csuk, R.; Glanzer, B. I. *J. Carbohydr. Chem.* **1990**, *9*, 809–822.
15. (a) Kraus, G. A.; Molina, M. T. *J. Org. Chem.* **1988**, *53*, 752–753. (b) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976–4978.
16. (a) Horton, D.; Periebe, W. *Carbohydr. Res.* **1981**, *94*, 27–41. (b) Czerneski, S.; Ville, G. *J. Org. Chem.* **1989**, *54*, 610–612. (c) Fuganti, C.; Serra, S. *Synlett* **1999**, 1241–1242.
17. Prepared from the corresponding 2,3,4,6-tetra-*O*-benzylpyranose by the oxidation with acetic anhydride and DMSO, see: Kuzuhara, H., Fletcher, Jr., H. G. *J. Org. Chem.* **1967**, *32*, 2531–2534.
18. Prepared by the modified method of Garegg's, see: Garegg, P., Hultberg, H. *Carbohydr. Res.* **1981**, *93*, C10–C11.
19. The compounds **7a–c** could also be prepared from the glycosidations of the corresponding 1-methylenesugars and methanol under the catalysis of TfOH (0.1 equiv.) following the procedure in Ref. 11.
20. Greene, T. W.; Wuts, P. G. M.; Eds., *Protective Groups in Organic Synthesis*; 2nd Ed., John Wiley and Sons, Inc.: New York, 1991; pp. 14–17.
21. Ding, X. L.; Wang, W.; Kong, F. Z. *Carbohydr. Res.* **1997**, *303*, 445–448.
22. Under strong acidic condition acetyl migration of **10** occurred. see (a) Ref. 11 and (b) Casinovi, C. G.; Framondino, M.; Randazzo, G.; Siani, F. *Carbohydr. Res.* **1974**, *36*, 67–73.
23. (a) Schauer, R. Chemistry, metabolism, and biological functions of sialic acids. In *Adv. Carbohydr. Chem. Biochem.*; Tipson, R. S., Horton, D., Eds.; Academic Press: New York, 1982; Vol. 40, pp 132–234. (b) Sharon, N.; Lis, H. *Science* **1989**, *246*, 227–234. (c) Crocker, P. R.; Kelm, S.; Dubois, C.; Martin, B.; McWilliam, A. S.; Shotton, D. M. J.; Paulson, C.; Gordon, S. *EMBO Journal* **1991**, *10*, 1661–1669. (d) Baumann, H.; Brisson, J. R.; Michon, F.; Pon, R.; Jennings, H. J. *Biochemistry* **1993**, *32*, 4007–4013.
24. (a) DeNinno, M. P. *Synthesis* **1991**, 583–593. (b) Okamoto, K.; Goto, T. *Tetrahedron* **1990**, *46*, 5835–5857. (c) Ito, Y.; Gaudino, J. J.; Paulson, J. C. *Pure Appl. Chem.* **1993**, *65*, 753–762. (d) Demchenko, A. V.; Boons, G. J. *Chem. Eur. J.* **1999**, *5*, 1278–1283.
25. Larcock, R. C., Ed., *Comprehensive Organic Transformations*; 2nd ed., John Wiley and Sons Inc.: New York, 1999; pp.1632–1634.
26. Marshall, J. A.; Garofalo, A. W.; Sedrani, R. C. *Synlett* **1992**, *643*, 645.